



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|----------------------------|-------------|----------------------|---------------------|------------------|
| 09/887,941 | 06/22/2001 | Mark L. Gonzalgo | 47675-21 | 8405 |
| 22504 | 7590 | 03/15/2005 | EXAMINER | |
| DAVIS WRIGHT TREMAINE, LLP | | | MYERS, CARLA J | |
| 2600 CENTURY SQUARE | | | | |
| 1501 FOURTH AVENUE | | | ART UNIT | PAPER NUMBER |
| SEATTLE, WA 98101-1688 | | | 1634 | |

DATE MAILED: 03/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) |
|------------------------------|------------------------|---------------------|
| | 09/887,941 | GONZALGO ET AL. |
| Examiner | Art Unit | |
| Carla Myers | 1634 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 22 February 2005.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 11-18 and 22 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 11-18 and 22 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on 22 June 2001 is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) Notice of References Cited (PTO-892)
2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____

4) Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ .
5) Notice of Informal Patent Application (PTO-152)
6) Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 22, 2005 has been entered.

Claims 11-18 and 22 are pending. All rejections not reiterated herein are hereby withdrawn. This action is made non-final.

Claim Rejections - 35 USC § 112

2. Claims 12-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The specification as originally filed does not provide basis for the concept set forth in the claims of dNTPs that are labeled with "radiolabels or fluorescent labels and combinations thereof" (claim 12) or any labeled dNTP (claims 13 and 14). The specification as originally filed provides basis for ³²P labeled dNTPs and basis for methods which utilize a combination of ³²P labeled dNTPs. The specification also states that fluorescent probes may be utilized in the disclosed method. However, there is no

basis in the specification to support the amendment to the claims to recite generically that the dNTPs are labeled with any combination of radiolabels and fluorescent labels. In particular, the specification states that fluorescent probes may be used "in place of a ^{32}P marker." The specification does not teach that fluorescent and radioactive labels may be used simultaneously in combination. Further, while the specification teaches the use of different ^{32}P labeled dNTPs, the specification does not provide support for the concept of using a combination of different radiolabels, such as ^{32}P labeled dNTPs in combination with ^{35}S labeled or ^{3}H labeled dNTPs. Further, claims 13 and 14 encompass the use of any label, such as enzyme, phosphorescent and mass labels. While the specification teaches the use of radioactive or fluorescent labels, the specification does not provide support for the broader concept of dNTPs labeled with any label.

Response to Arguments:

In the response, Applicants point out that page 9 of the specification "discloses and teaches the concept of using other labels 'instead of a ^{32}P marker.' Given this teaching, Applicants conclude that "one of ordinary skill in the art at the time of filing would understand from the instant teachings that the dNTPs could be labeled in any manner that would allow for determination of the first primer-extended base."

Applicant's arguments have been fully considered but are not persuasive. The present rejection is not premised on the question of whether the specification enables the use of different labels to detect the first primer extended base, but whether the specification as originally filed provides basis for using a combination of radioactive and

fluorescent labels or provides basis for the use of any label. While the specification teaches that either radioactive or fluorescent probes may be used in the present methods and teaches using different ³²P-labeled dNTPs, the specification as originally filed does not provide basis for the concept of using a combination of radioactive and fluorescent labels or a combination of different types of radioactive or fluorescent labels. Further, the teachings in the specification of two specific types of labels, i.e., fluorescent and radioactive, does not provide basis for the broader concept of any type of label, as encompassed by claims 13 and 14.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 13 and 14 are indefinite over the recitation of "the labeled dNTP" because this phrase lacks proper antecedent basis. While the claims previously refer to dNTPs, the claims do not previously refer to labeled dNTPs.

Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 11-18, and 22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 6,251,594. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims and the claims of '594 are inclusive of methods of determining the DNA methylation status of a genomic DNA sample by assaying for the methylation state at the cytosine residue of the CpG dinucleotide sequences by measuring the incorporation of labeled dNTPs. The present claims recite generally that the dNTPs are labeled, whereas the claims of '594 specifically recite labeling the dNTPs with ^{32}P . Accordingly, the presently claimed method encompasses detecting the use and detection of ^{32}P -labeled dNTPs. Additionally, both the present claims and the claims of '594 encompass Ms-SNuPE primers comprising SEQ ID NO: 1-12.

Response to Arguments:

In the response, Applicants state that the present application is commonly owned with the '594 patent and that applicants will file a terminal disclaimer upon the Examiner's indication of allowable subject matter. Accordingly, the rejection is maintained for the reasons of record until the filing of an appropriate terminal disclaimer.

5. Claims 11-18, and 22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 6,811,892 (Application No. 10/109,725) Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims and the claims of '892 are inclusive of methods of determining the DNA methylation status of a genomic DNA sample by assaying for the methylation state of more or more CpG dinucleotide sequences within a sequence that hybridizes to any one of SEQ ID NO: 1-12.

Response to Arguments:

In the response, Applicants state that the present application is commonly owned with the '892 patent and that applicants will file a terminal disclaimer upon the Examiner's indication of allowable subject matter. Accordingly, the rejection is maintained for the reasons of record until the filing of an appropriate terminal disclaimer.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (571) 272-0747. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571)-272-0745.

The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866)-217-9197 (toll-free).

Carla Myers
March 9, 2005

Carla Myers
CARLA J. MYERS
PRIMARY EXAMINER